PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P030349WO	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB 03/01684	International filing date *(day/month/year)* 17.04.2003	Priority date *(day/month/year)* 17.04.2002
International Patent Classification (IPC) or both national classification and IPC C07K16/00		
Applicant EUROPEAN MOLECULAR BIOLOGY LABORATORY et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
17.11.2003	13.05.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Bayer, A Telephone No. +49 89 2399-7103

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/01684

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-25 as originally filed

Claims, Numbers

1-26 as originally filed

Drawings, Sheets

1/10-10/10 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 17,20-26

   because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 17,20-26

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/ or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-15,18,19
	No:	Claims	16
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-16,18,19
Industrial applicability (IA)	Yes:	Claims	1-16,18,19
	No:	Claims	

2. Citations and explanations

   see separate sheet

1. Reference is made to the following documents:

D1: WO 9633735 A

D2: TEMPLIN MF ET AL: 'PROTEIN MICROARRAY TECHNOLOGY', TRENDS IN BIOTECHNOLOGY, 2002-04-01, , vol. 20, no. 4, pages 160 to 166

D3: LUEKING A ET AL: 'PROTEIN MICROARRAYS FOR GENE EXPRESSION AND ANTIBODY SCREENING', ANALYTICAL BIOCHEMISTRY, 1999-05, , vol. 270, no. 1, pages 103 to 111

D4: WO 0114425 A

D5: HAAB B ET AL: 'PROTEIN MICROARRAYS FOR HIGHLY PARALLEL DETECTION AND QUANTITATION OF SPECIFIC PROTEIN AND ANTIBODIES IN COMPLEX SOLUTIONS', GENOME BIOLOGY, 2001, , vol. 2, no. 2, pages COMPLETE to

D6: ARENKOV P ET AL: 'PROTEIN MICROCHIPS: USE FOR IMMUNOASSAY AND ENZYMATIC REACTIONS', ANALYTICAL BIOCHEMISTRY, 2000-02-15, , vol. 278, no. 2, pages 123 to 131

2. Having regard to the documents above (see 1.) the subject-matter of the claims searched of the present application does not seem to be inventive (**Article 33(3) PCT**):

The present application refers to the production of monoclonal antibodies wherein the method claimed encloses the routine procedure on generating monoclonal antibodies as can be seen from e.g. D1 which is regarded as closest prior art. This document teaches the generation of monoclonal antibodies including the selection/screening of the hybridomas produced using a sandwich ELISA wherein the antigen is coated on microtiter plates (see e.g. page 9 line 26-page 10 line 17). D1 does not disclose the selection/screening of the hybridomas using a protein (antigen chip), the underlying problem of the present application is thus an alternative method on hybridoma selection/screening, the solution being the use of protein (antigen) chips. However the use of antigen chips (microarray technology) for the selection/detection of antibodies as well as the advantages of microarray technology (like e.g. high-throughput screening, miniaturizing of assays, parallel analysis, multianalyte analysis) over known immunoarrays like sandwich ELISA are already known from D2-D6:

D2 reviews the development of microarray technology, specifically protein microarrays, including the application in antigen-antibody binding and miniaturizing of sandwich immunoassays (see e.g. page 165 left-hand column last paragraph).
D3 teaches the use of protein microarray (chip) for high-throughput antibody specifity screening (see e.g. page 110 "conclusions").
D4 refers to the use of protein/antigen chips in high-throughput screening/detection of antibodies for the diagnosis of diseases (see e.g. page 7 lines 7-20, page 11 lines 10-12).
D5 shows that protein microarrays are suitable for parallel detection and quantification of specific antibodies in solutions (see e.g. page 2 right-hand column last paragraph-page 5 left-hand column first paragraph).
D6 shows the use of either antigens or antibodies on microchips and their use in immunoassays for e.g. parallel analysis (see e.g. abstract, page 126 left-hand column second paragraph- page 127 left-hand column first paragraph)

The person skilled in the art, having in mind the advantages of microarray technology from D2 (or one of D3-D6) and the knowledge of D1, would be highly motivated to apply this technology thus combining both D1 and D2 (or one of D3-D6) to arrive in an obvious manner to the subject matter of the present application.

3. In the light of D1 claim 16 does not appear to be novel (**Article 33(2) PCT**):

Claim 16 refers to the production of an immortalised cell line. However the method claimed encloses the normal routine procedure on the production of hybridomas as can be seen for e.g. in D1. The only difference between D1 and the method claimed is the selection procedure for the produced immortalised cell line and not the method of production itself and thus D1 is novelty destroying for claim 16. Additionally, even if the applicant could prove the novelty of this claims, it is not considered as being inventive having regard to the argumentation above (see 2.) since the selection/screening of an antibody directly leads to the identification/selection of the antibody producing hybridoma.